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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DESAI, ANAND U	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 11/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/661,156	SATO ET AL.	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *September 18, 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27,32,53,54,76,78,158,175 and 195* is/are pending in the application.

4a) Of the above claim(s) *1-9,11,12,27,32,53,54,76,158,175 and 195* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,13-26 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20040714, 20060131, 20060727*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

Election/Restrictions

2. Applicant's election with traverse of Group I, claims 1-27, 54, 76, 78, and 175, drawn to an isolated polypeptide, and drawn to a polypeptide conjugated to a detectable label in the reply filed on September 18, 2006 is acknowledged. The traversal is on the ground(s) that selection of a single sequence is unreasonable. Applicant cites M.P.E.P. 803.4 to state that normally ten sequences constitute a reasonable number for examination purposes. Applicant further elects sequences SEQ ID NOs: 304-310, and 356 for examination. Applicant states that if restriction requirement is maintained then SEQ ID NO: 310 is elected for searching purposes as a designated subset of the sequences.

The selection of a single amino acid sequence is not unreasonable, because the sequences have different structures that would necessarily confer different functions. In addition, it is noted that M.P.E.P. 803.4 states that up to ten independent and distinct nucleotide sequences can be examined without restriction. Furthermore, as stated in M.P.E.P. 803.4, the complex nature of protein amino acid sequences may necessitate that the reasonable number of sequences to be selected be less than ten.

Clarification is requested as to whether Applicant is stating that SEQ ID NO: 310 is considered to be an obvious variant of the sequences. SEQ ID NO: 310 is being considered to be

an obvious variant of SEQ ID NO: 304-310, and 356, since Applicant state SEQ ID NO: 310 is a designated subset of the sequences for searching purposes.

Claims 1-9, 11, 12, 27, 32, 53, 54, 76, 158, 175, and 195 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 18, 2006.

The requirement is still deemed proper and is therefore made FINAL.

Claims 10, 13-26, and 78 are currently pending and are under examination.

Priority

3. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(e). The priority date is March 1, 2002.

Information Disclosure Statement

4. The information disclosure statements (IDSs) submitted on July 14, 2004, January 31, 2006, and July 27, 2006 are being considered by the examiner.

Specification

5. The disclosure is objected to because of the following informalities:

6. Suggest updating the related applications section on page 1. State current status of copending applications, which is now abandoned.

7. In the brief description of the drawing section, the abbreviation for "JJ" is described in figure 3. Suggest describing the abbreviation for spacer "JJ" at first occurrence in figure 1.

8. On page 34, line 1, the SEQ ID NO: identifier next to the amino acid sequence disclosed is missing.

9. On page 152, the title in experiment A has a typographical error. There is an unnecessary dash between the letter "m" and RNA.

10. On pages 153, and 161, the description of Celsius has a typographical error. Suggest, "°C" as disclosed on page 156.

11. On page 177, line 12, there is a typographical error. The Celsius identifier is inadvertently superscripted.

12. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Appropriate correction is required.

Claim Objections

13. Claim 14 is objected to because of the following informalities:

14. In claim 14, the article describing the second Markush member, amide bond substitution, has a typographical error. The "and" appears to be intended to be "an".

Appropriate correction is required.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claim 78 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, and 11-20 of copending U.S. Patent Application Publication US 2004/0018974 A1 (SN 10/379,287). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending application are drawn to a compound comprising a polypeptide sequence that is encompassed by claim 78, and can bind to the same tyrosine kinase receptor, KDR, and the ligand-receptor complex, KDR/VEGF.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

19. In claim 10, suggest describing/spelling out KDR, and VEGF at first occurrence in the claim. What do the abbreviations KDR and VEGF describe?

20. In claim 10, it appears as though Lin20 is used to identify different sequences. What is Lin20 identifying? As well, suggest describing/spelling out Lin20 at first occurrence in the claim.

21. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

22. Claims 10, 13-26, and 78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

MPEP § 2163 further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163 does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two

chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention.* Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

In the instant case, the claims are drawn to an isolated polypeptide having the ability to bind to kinase insert domain-containing receptor (KDR) or vascular endothelial growth factor(VEGF)/KDR complex comprising an amino acid sequence with a consensus sequence identified as Z_1-X_1-X_2-X_3-X_4-X_5-Z_2 that further comprises N-terminal and/or C-terminal flanking peptides of one or more amino acids. The isolated polypeptide can also comprise modifications selected from a group consisting of an amino acid substitution, an amid bond substitution, a D-amino acid substitution, a glycosylated amino acid, a disulfide bond, a disulfide mimetic substitution, an amino acid translocation, a retroinverso peptide, a peptoid, a retro-inverso peptoid, and a synthetic peptide. The isolated peptide is also conjugated to one or more detectable labels, optionally further comprising a linker or spacer between the polypeptide and the detectable label. The detectable label can further comprise a chelator. Claim 78 is drawn to a multimeric polypeptide construct having the ability to bind to KDR or VEGF/KDR complex comprising an amino acid sequence with a consensus sequence identified as Z_1-X_1-X_2-X_3-X_4-X_5-

Z_2 that can further comprises N-terminal and/or C-terminal flanking peptides of one or more amino acids.

(1) Level of skill and knowledge in the art: (2) Partial structure: (3) Physical and/or chemical properties: (4) Functional characteristics: (5) Method of making the claimed invention:

The level of skill required for generation of peptide pharmaceutical is high, and the knowledge in the art related to molecular mechanisms of angiogenesis can be characterized as being in the early adolescent stages of maturation. The specification describes the method of identifying peptides that can bind a KDR receptor and/or a KDR/VEGF complex by using bacteriophage display bio-panning techniques. The specification describes in vitro cell binding assays to disclose the binding of peptide fragments to the KDR/VEGF complex. The specification describes the production of conjugates and dimers of peptide fragments using reactive lysine residues and standard peptide chemistry cross-linkers.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad genus. The claims encompass an isolated polypeptide, wherein the variables Z_1 and Z_2 are any polypeptides of at least one amino acid. Claim are broadly generic to all possible polypeptides, which also include any modifications, such as any amino acid substitution as encompassed by the claims. The possible variations are enormous to any class of isolated polypeptide. Since the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the modified polypeptide

beyond those disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. The specification does not disclose multiple species of Z_1 or Z_2 polypeptides that can be linked to the polypeptide, which will not alter the functional ability of binding KDR or VEGF/KDR complex.

While having written description of isolated polypeptides identified in the specification tables and/or examples, the specification is devoid of all modified polypeptides that qualify for the functional characteristics claimed.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

24. Claims 10, 13, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Bittle et al. (U.S. Patent 4,544,500).

Bittle et al. describe a peptide sequence that comprises the sequence Ala-Gln-Lys-Val-Ala. The peptide encompasses the consensus sequence disclosed in claim 10. The peptide comprises amino acid residues N-terminal to the Ala residue, and C-terminal to the carboxy-terminal Ala residue (see claim 3). It is recognized that the structure of a peptide sequence confers function, and therefore since the peptide meets the structural limitations it must necessarily and inherently have the functions being claimed.

25. Claims 10, and 13-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Soker et al. (Journal of Biological Chemistry 272(50): 31582-31588 (1997)).

Soker et al. describe purified peptides, $VEGF_{121}$, $VEGF_{165}$, and glutathione S-transferase fusions comprising different segments of exon 7 and exon 8 of VEGF (see page 31583, Experimental Procedures, Materials section, and Preparation of GST-VEGF Exon 7 and 8 Fusion Proteins section). Soker et al. describe the radioiodination of VEGF using ^{125}I (see page 31583, Experimental Procedures, Radioiodination of VEGF section). The VEGF peptide segment of the fusion peptides can also be interpreted to encompass the isolated polypeptide that comprises a modification as disclosed in claim 14. It is recognized that the structure of a peptide sequence confers function, and therefore since the peptide meets the structural limitations it must necessarily and inherently have the functions being claimed.

26. Claims 10, and 13-26 are rejected under 35 U.S.C. 102(e) as being anticipated by Wescott et al. (U.S. Patent 6,984,373 B2).

Wescott et al. describe a polypeptide comprising the sequence, Trp-Ala-Pro-Cys-Gln-**Glu-Glu-Pro-Trp-Leu**-Phe-Cys-Phe-His-Gly (SEQ ID NO: 6), which encompasses the consensus sequence disclosed in claim 10 (see bold segment). The polypeptide can be linked to at least one paramagnetic metal atom. The polypeptide can be linked to a detectable label (see claims 5, 9, 18, 21, and 25-29). The polypeptide can be labeled with a fluorinated gas (see col. 23, lines 18-30). It is recognized that the structure of a peptide sequence confers function, and therefore since the peptide meets the structural limitations it must necessarily and inherently have the functions being claimed.

Conclusion

27. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on (517) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

October 24, 2006

ROBERT A. WAX
PRIMARY EXAMINER